Appl. No. 10/815,449

Filed: April 1, 2004

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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the

application:

**Listing of Claims:** 

1. (currently amended) An A human or humanized antibody which binds to IGF-IR

wherein said antibody inhibits the binding of IGF-I and IGF-II to IGF-IR, and further

wherein said antibody

a) is of a lgG1 isotype, and;

b) shows a ratio of <u>IC50s for the</u> inhibition of the binding of IGF-I and IGF-II to IGF-

IR of 1:3 to 3:1, ;and further

c) induces cell death of 20% or more cells of a preparation of IGF-IR expressing

cells after 24 hours at a concentration of 100 nM of said antibody in an antibody

dependent cellular toxicity assay.

2. (currently amended) The antibody of claim 1, characterized in that wherein said

antibody induces death of 20% or more cells of a preparation of IGF-IR expressing cells

after 4 h at an antibody concentration of 100 nM of said antibody in a complement

dependent cytotoxicity (CDC) assay.

3. (canceled)

4. (currently amended) The antibody of claim 1, wherein said antibody binds to the

IFG-IR IGF-IR with an affinity of about 10<sup>-11</sup> to 10<sup>-8</sup> M (K<sub>D</sub>).

5. (currently amended) The antibody of claim 1, wherein said antibody binds to the

IFG-IR IGF-IR with an affinity of about 10<sup>-11</sup> to 10<sup>-9</sup> M (K<sub>D</sub>).

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- 6. (original) The antibody of claim 1, wherein said antibody further comprises complementarity determining regions (CDRs) having the following sequences:
- a) an antibody heavy chain having CDRs comprising CDR1 (aa 31-35), CDR2 (aa 50-66) and CDR3 (aa 98-108) of SEQ ID NO:1, wherein amino acid 31 can be asparagine or serine, amino acid 66 can be glycine or can be deleted, and amino acid 104 can be glutamic acid or aspartic acid; and
- b) an antibody light chain having CDRs comprising CDR1 (aa 18-34 or aa 24-34), CDR2 (aa 50-56) and CDR3 (aa 89-98) of SEQ ID NO:2, wherein amino acid 96 can be proline or isoleucine, and amino acid 98 can be phenylalanine or can be deleted.
- 7. (original) An antibody according to claim 1, wherein said antibody further comprises:
- a) a heavy chain comprising a variable region (VH) of SEQ ID NO:1, wherein amino acid (aa) 30 is serine or arginine, aa 31 is asparagine or serine, aa 94 is histidine or tyrosine and aa 104 is aspartic acid or glutamic acid, further comprising a human heavy chain constant region (CH); and
- b) a light chain comprising a variable region (VL) of SEQ ID NO:2, wherein aa 96 is proline or isoleucine, aa 100 is proline or glutamine, aa 103 is arginine or lysine, aa 104 is valine or leucine and aa 105 is aspartic acid or glutamic acid, and further comprising a human light chain constant region (CL).
- 8. (original) The antibody of claim 7, wherein the heavy chain amino acids 30, 31, 94, and 104 are the following:
  - a) aa 30 Arg, aa 31 Asn, aa 94 Tyr and aa 104 Asp, or
  - b) aa 30 Arg, aa 31 Ser, aa 94 Tyr and aa 104 Asp, or
  - c) aa 30 Ser, aa 31 Asn, aa 94 His and aa 104 Glu.
  - 9. (original) The antibody of claim 7, wherein the light chain amino acids 96, 100, 103, 104 and 105 are the following:
  - a) aa 96 Pro, aa 100 Pro, aa 103 Lys, aa 104 Val and aa 105 Asp, or
  - b) aa 96 lle, aa 100 Gln, aa 103 Arg, aa 104 Leu and aa 105 Glu.

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10. (original) The antibody of claim 1 wherein said antibody is obtainable from a hybridoma cell line consisting of the group selected from <IGF-1R> HuMab Clone 1a, <IGF-1R> HuMab Clone 23 and <IGF-1R HuMab Clone 8.

11. (currently amended) A pharmaceutical composition comprising said the antibody of claim 1 wherein said antibody is present in said pharmaceutical composition in a pharmaceutically effective amount and a pharmaceutically acceptable carrier or diluent.

Claims 12 to 22 (canceled)

23. (new) A composition comprising the antibody of claim 6 and a pharmaceutically acceptable carrier or diluent.